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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,937	11/28/2001	David M. Anderson	05900002AA	7327

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Whitham, Curtis & Christofferson, PC
11491 Sunset Hills Road - #430
Reston, VA 20190

EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/994,937	ANDERSON, DAVID M.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-68 and 70-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-68 and 70-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed and Declaration under 37 CFR 1.132 on December 15 2009 is acknowledged. Claims 1-65 and 69 were/stand cancelled. Claims 70-111 were added. Claims 66-68 were amended. Claims 66-68 and 70-111 are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments and Rule 132 Declaration

The arguments and declaration under 37 CFR 1.132 filed December 15 2009 is sufficient to overcome the rejections of claims 1, 3-16, 18, 27, 29-41, 43, 52-53, 56, 59, 66 and 68-69 under 35 U.S.C. 103(a) as being unpatentable over Engstrom et al. (US Patent No. 5151272) in view of Unger et al. and claims 17, 25-26, 42 and 50-51 under 35 U.S.C. 103(a) as being unpatentable over Engstrom et al. in view of Yamakawa et al.

Claim Objections

Claim 72 is objected to because of the following informalities: the claim recites "greater that" instead of "greater than". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 68, 83-89, 92, 94, 97, 101, 108-111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 68, 101 and 108-111 introduce new matter as the claims recite the limitation: "crystalline phase structured fluid which exists at body temperature". There is no support in the specification for this limitation. The limitation of: the crystalline phase existing at body temperature was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The specification discloses that the cubic phase was capable of solubilizing dantrolene sodium at body temperature but does not describe the instantly claimed limitation (experiment 1 where applicant indicates support can be found). While this suggests that the cubic phase is capable of solubilization at body temperature, this does not indicate that the cubic phase necessarily exists at body temperature. Therefore, it is the Examiner's position that the disclosure does not

reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Claim 72, 79 and 85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 72, 79 and 85 introduce new matter as the claims recite the limitation: "pharmaceutical active is greater than 5% soluble in said essential oil ". There is no support in the specification for this limitation. The limitation of the pharmaceutical agent being greater than 5% soluble in the essential oil was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The specification discloses that paclitaxel is soluble at specific percentages in specific oils. While these percentages are greater than 5%, this does not support the limitation for all pharmaceutical actives being greater than 5% soluble in the essential oil nor does it support paclitaxel being soluble in all values above 5% in the essential oils. Support is only for a specific drug (paclitaxel) as specific concentrations. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66, 68, 70-71, 73-74, 83-84, 86-87, 90, 92, 95, 97-98, 100-104, 106, 108, 110 rejected under 35 U.S.C. 102(b) as being anticipated by Anderson (WO 9912640, cited in the Office action mailed on 6/16/09) as evidenced by Evans (US Patent No. 5026548), Burdock (Food and Color Additives, 1997) and Muldoon et al. (Systematic Organic Chemistry, 1957).

Anderson et al. exemplify a cubic phase liquid crystal formulation comprising soy lecithin (epikuron 200) in 0.345 g, anisole in 0.357 g, water and Paclitaxel.

As evidenced by Evans et al., Epikuron 200 is fractionated soya lecithin containing 92% phosphatidylcholine (column 12, lines 13-14).

As evidenced by Muldoon et al., anisole is found in anise oil (page 567). As evidenced by Burdock, anisole can be chemically synthesized as well as found in natural sources such as olive, artichoke, vanilla, etc. (page 178-179, anisole section).

Therefore, Anderson exemplify a composition comprising a cubic phase, water, phospholipid, component of essential oil and a pharmaceutical active.

Regarding the claimed ratio of phospholipid to essential oils or component thereof. The ratio exemplified is 0.97 to 1.

Response to Arguments

Although this rejection was not recited in the last Office action, the examiner would like to address applicant's arguments as they pertain to this rejection.

Applicant argue that anisole is not an essential oil. Applicants submitted the term anisole from Wikipedia and Merck index which show the chemical synthesis of anisole. It was argued that all preparations for anisole are synthetic and no natural source is cited.

While the examiner does not disagree that anisole can't be synthetically made (it clearly can), Muldoon et al. states that anisole is found in anise oil and Burdock clearly shows that while it can be chemically synthesized it is also found in nature. Therefore, the examiner disagrees that anisole is not at leas a component of anise oil.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 67, 72, 75-82, 85, 88-89, 91, 93-94, 96, 99, 105, 107, 109 and 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson as evidenced by Evans, Burdock and Muldoon et al.

Applicant Claims

The instant application claims a composition comprising A) a reversed cubic liquid phase comprising water; a phospholipid; tocopherol, and B) a pharmaceutical active solubilized in said structured fluid.

The instant application claims a composition comprising A) a reversed cubic liquid phase comprising water; a phospholipid; an essential oil or component thereof or tocopherol, and B) a pharmaceutical active solubilized in said structured fluid.

Specific essential oils claimed include anise oil and peppermint.

Specific drug claimed include daunorubicin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Anderson is directed to coated particles that comprise an internal core comprising a matrix and an exterior coating. The nanostructured liquid crystalline phase material may be formed form a polar solvent, a surfactant and an amphiphile or hydrophobe (page 34, lines 7-11). Example 36 comprises Paclitaxel, eugenol, soy lecithin (epikuron 200) and glycerol. Example 37 comprises soy lecithin (epikuron 200), anisole, water and Paclitaxel. The preferred amphiphile and hydrophobe components (third component) include anise oil, clove oil, peppermint oil; eucalyptus oil; eugenol;

vitamin E, etc. (pages 37-38 lines 29-32 and 1-4). Examples of active agents when can be solubilized besides paclitaxel include daunorubicin (page 45, line 22)

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

While Anderson teach preferred third components include anise oil, peppermint oil and vitamin E, Anderson does not exemplify formulations with these components.

While Anderson teach that the drug delivered can be daunorubicin, Anderson do not exemplify formulations with daunorubicin.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention formulate a composition wherein the paclitaxel is dissolved in water, phospholipid and tocopherol or an essential oil such as anise oil or peppermint oil. One of ordinary skill in the art would have been motivated to utilize these three components for solubilizing paclitaxel as Anderson teaches that the nanostructured liquid crystalline phase material may be formed from a polar solvent, a surfactant and an amphiphile or hydrophobe and exemplify a formulation comprising water (polar solvent), soy lecithin (phospholipid, surfactant) and anisole (amphiphile or hydrophobe). Therefore, it would have been obvious to one of ordinary skill in the art to substitute the exemplified amphiphile or hydrophobe with other preferred hydrophobes such as tocopherol or essential oils like anise oil or peppermint oil. It would have been obvious to one of ordinary skill in the art to try any of the specifically taught preferred third components as a person with ordinary skill has good reason to pursue known options within his or her

technical grasp. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the exemplified drug Paclitaxel for other specifically taught drugs such as daunorubicin. It would have been obvious to one ordinary skill in the art to vary the drug in the formulation depending on the disease or condition to be treated. Therefore, one of ordinary skill in the art would have been motivated to utilize daunorubicin in place of the exemplified paclitaxel when desiring to deliver an antibiotic.

Regarding the claimed ratio of phospholipid to tocopherol, the exemplified ratio of phospholipid to third component is 0.97 to 1. Since tocopherol is an alternative third component it would have been obvious to utilize it in the same amount as the exemplified third component.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments/Declaration under Rule 132

Applicant argues that (1) anisole is not an essential oil or component thereof. Applicant argues that (2) *in re Kubin* states that obvious to try is erroneously applied with what would have been obvious to try would have been to vary all the parameters or

teach each of numerous possible choices until one possibly arrived at a successful results. It is argued that Anders is not a proper 103(a) reference because the selection of the defined components of the composition was made form many choices which are not emphasized.

Applicant's arguments filed December 15 2009 have been fully considered but they are not persuasive.

Regarding applicant's first argument, the examiner addressed this argument above. Specifically, while the examiner does not disagree that anisole can be synthetically made (it clearly can), Muldoon et al. states that anisole is found in anise oil and Burdock clearly shows that while it can be chemically synthesized it is also found in nature. Therefore, the examiner disagrees that anisole is not at leas a component of anise oil.

Regarding applicants' second argument, the examiner disagrees. The only variable is the third component (amphiphile or hydrophobe). The polar solvent and phospholipid exemplified are the same as instantly claimed. Therefore, one would just be varying the third component. Anderson emphasizes certain third components which are preferable. Anderson points to 50 specific preferred third components. Additionally, the list is finite as there is clearly a beginning and end point. Furthermore, out of that 50, at least 10 are an essential oil or tocopherol. More may possibly read on component thereof, the examiner just did not spend the time to determine exactly how many would be considered components thereof (such as menthol and cinnamaldehyde).

In his Declaration Dr. Anderson argues that anisole is not an essential oil. Dr. Anderson additionally argues that the incorporation of the drug in the material is metastable and leaves only very low loading of the drug whereas the instant invention allows for high loadings.

The declaration under 37 CFR 1.132 filed December 15 2009 is insufficient to overcome the rejection.

The issue of anisole and essential oil is addressed above. The arguments made by Dr. Anderson are not commensurate in scope. The examiner maintains that it would have been obvious to one of ordinary skill in the art to vary the third component from the finite list taught in Anderson thereby replacing the essential oil component anisole with other third components like anise oil or peppermint oil or vitamin E. While example 36 indicates that the formulation was metastable it also states it possessed a loading of 3 wt.% (which is also indicated as high) and that the precipitation is very slow. Therefore, clearly some of the paclitaxel is dissolved and would read on the claims.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

/Mina Haghighatian/
Primary Examiner, Art Unit 1616